

Appl. No. 09/929,863
Amtd. Dated August 21, 2003
Reply to Office action of March 12, 2003

IN THE CLAIMS:

Claim 1. (Currently amended) A method to induce differentiation of a an isolated or purified naïve CD4⁺ T cell to a Tr1 cell comprising contacting the naïve CD4⁺ T cell with an appropriate amount of interferon- α (IFN- α) and an appropriate amount of IL-10.

Claim 2. (Currently amended) The method of Claim 1, wherein said Tr1 cell is characterized by:

- a) CD4 expression;
- b) high levels of IL-10 production;
- c) significant levels of TGF- β or IFN- γ production; and
- d) little or no production of IL-4 or IL-2.

Claim 3. (Currently amended) The method of Claim 2, wherein:

- a) said high level of the IL-10 production is at least 6000 pg in 1 ml for 10⁶ cells in 48 h;
- b) said significant level of the TGF- β production is at least 600 100 pg in 1 ml for 10⁶ cells in 48 h;
- c) said significant level of the IFN- γ production is at least 1000 400 pg in 1 ml for 10⁶ cells in 48 h;
- d) said little or no the IL-4 production is less than 200 pg in 1 ml for 10⁶ cell in 48 h; or
- e) said little or no the IL-2 production is less than 200 pg in 1 ml for 10⁶ cell in 48 h;

when evaluated from cultures of about 10⁶ cells per ml per 48 hours.

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Claim 4. (Currently amended) The method of Claim 2, wherein:

- a) ~~said high level of the IL-10 production is at least 6000~~ ~~12000~~ pg in 1 ml for ~~10⁶ cells in 48 h~~;
- b) ~~said significant level of the TGF-β production is at least 600~~ pg in 1 ml for ~~10⁶ cells in 48 h~~;
- c) ~~said significant level of the IFN-γ production is at least 1000~~ pg in 1 ml for ~~10⁶ cells in 48 h~~;
- d) ~~said little or no the IL-4 production is less than 200~~ ~~100~~ pg in 1 ml for ~~10⁶ cell in 48 h~~; or
- e) ~~said little or no the IL-2 production is less than 200~~ ~~100~~ pg in 1 ml for ~~10⁶ cell in 48 h~~;

when evaluated from cultures of about 10⁶ cells per ml per 48 hours.

Claim 5. (Original) The method of Claim 2, wherein said Tr1 cell:

- a) has a reduced proliferative potential in response to polyclonal activation; and/or
- b) suppresses response to alloantigens by responder T cells.

Claim 6. (Currently amended) The method of Claim 1, wherein said Tr1 cell cell suppresses antigen-specific activation of a naive autologous T cells cell.

Claim 7. (Original) The method of Claim 5, wherein said suppressed response to alloantigens is mediated by IL-10 and/or TGF-β.

Claims 8-10. (Cancelled).

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Claim 11. (Original) The method of Claim 1, wherein said contacting is in combination with an antigen.

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Claim 12. (Original) The method of Claim 11, wherein said antigen is an alloantigen.

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Claim 13. (Currently amended) The method of Claim 1, wherein said Tr1 cells are cell
is further proliferated in IL-15.

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Claim 14. (Currently amended) The method of Claim 1, wherein said Tr1 cells are cell
is further tested for antigen specificity.

Claims 15-18. (Cancelled).

Claim 19. (New) A method to induce differentiation of an isolated or purified cord blood
T cell to a Tr1 cell comprising contacting the cord blood cell with an appropriate amount
of IFN- α .